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The effects of calcium alginate on wound healing

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Summary

A non-woven alginate dressing has been used on experimental, full and partial thickness wound models for periods up to 14 days, to assess its effects on wound healing. Histological evaluation has shown that it is an effective haemostat, generally well tolerated by body tissues. Good epidermal healing was seen on all wounds although cellular reactions could be provoked in full thickness wounds without occlusion, if there was an insufficient volume of wound exudate to completely wet the alginate fibres.

Introduction

Alginates are highly absorbent, gel-forming materials with haemostatic properties *(1)* and it has long been known that more rapid wound healing occurs when a gel is formed at the wound surface and dehydration is prevented *(2)*. In contact with body fluids, alginates are known to break down to simple monosaccharide-type residues and be totally absorbed. The wound exudate converts the calcium to the sodium salt facilitating the removal of the dressing by dissolution. Any residual fibres remaining within the wound are biodegradable thus eliminating the need for complete removal *(3)*.

A recent paper by Groves and Lawrence *(4)* has shown that significant haemostasis can be obtained when calcium alginate is applied to graft donor sites in the immediate post-surgery phase. Calcium alginate was left *in situ* for five minutes on each wound and then removed. As Groves and Lawrence point out, further work is required on the effects of prolonged contact of alginate with body fluids. Our studies show the histology of wounds exposed to calcium alginate, with and without occlusion, for periods between one and fourteen days. These wounds were not redressed at any stage, nor were dressings removed prior to wound biopsy. This ensured that repair tissue remained undisturbed.

Materials and methods

Calcium alginate non-woven fabric was supplied by the manufacturers Courtaulds plc. This is the same as the material used by NI Medical in the production of Sorbsan®. The supplied fabric was cut to the required sizes and sterilised by gamma irradiation (3.0 Mrads).

All trials were carried out using pedigree Large White domestic pigs, since the skin of this animal more closely resembles that of man than that of any other commonly used laboratory animal *(5)*, using the methods described by Winter and Clarke *(6)*.

Two wound models were used, (1) the partial thickness wound measuring 2.5 cm×2.5 cm×0.5 mm in which the epidermis and papillary layer of the dermis are completely excised and, (2) the full thickness wound measuring 2.5 cm×2.5 cm×8.0 mm in which tissue is dissected to a level within the subcutaneous fat. The alginate dressing was compared to Op-Site® and a control gauze covering. Table I gives details of the wound type, time of assessment and dressings allocated to each animal.

Measurements of epidermal regeneration were made for all partial thickness wounds using a method based on that described by Simpson and Winter *(7)*.

Results

Calcium alginate (1-ply) on partial thickness wounds at 3 days. All wounds had suffered some dehydration by 3 days where no further cover to prevent moisture loss was used. Wounds suffering less dehydration showed a faster rate of re-epithelisation (Fig. 1a). In all wounds the exudate had penetrated throughout the dressing and leucocytes (predominantly polymorphoneucleocytes) were seen lying in close proximity to the calcium alginate, which had provoked no abnormal cellular response. The control wounds, which had no dressing, had the typical appearance of a 3 day wound with epidermis migrating beneath a dehydrated layer of dermis and leucocytes.

Where calcium alginate was used with occlusion, wound repair was at a mature stage by 3 days (Fig. 1b), with epidermis, 5–8 cells thick migrating through moist exudate. On the control wounds, that is Op-Site® alone, the epidermis was only 2–5 cells thick. Indication of early connective tissue repair, that is blood vessel ingrowth, could be seen. There was also an apparently greater leucocytic response to the calcium alginate compared to the control wounds (Figs. 2 and 3).

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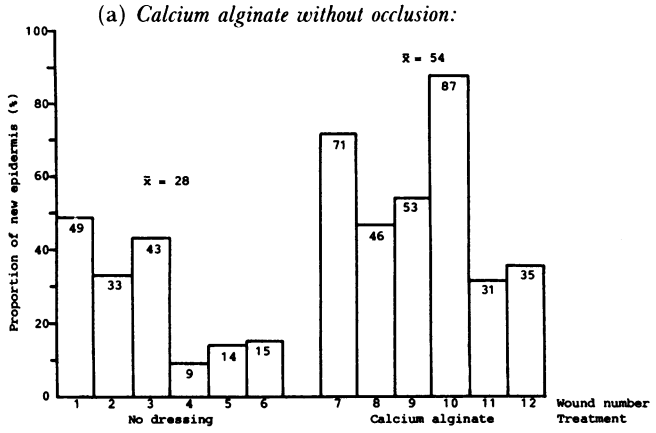
TABLE I *Wounds used in the study of calcium alginate*

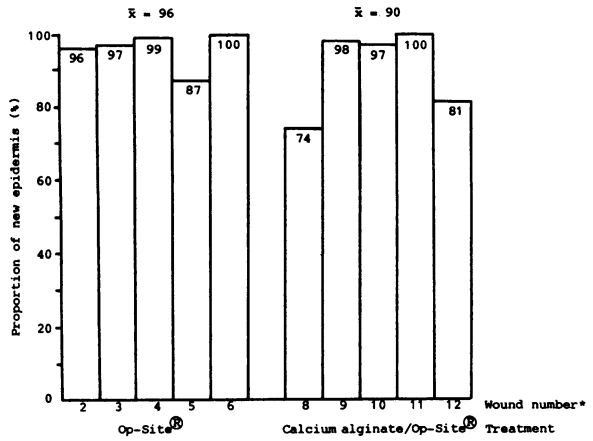
Experiment	*Number of wounds and treatment*	*Biopsy time*
1 Calcium alginate on partial thickness wounds without occlusion	6 wounds ; no dressing* 6 wounds ; one layer of calcium alginate	3 days
2 Calcium alginate on partial thickness wounds with occlusion	6 wounds ; Op-Site® dressing* 6 wounds ; one layer calcium alginate covered with Op-Site®	3 days
3 Calcium alginate in full thickness wounds without occlusion, to test haemostatic effect	6 wounds ; covered with four-ply cotton gauze* 6 wounds ; filled with six layers of calcium alginate and covered with four-ply cotton gauze	1 day
4 Calcium alginate in full thickness wounds without occlusion, to test long-term effects on connective tissue repair	6 wounds ; covered with four-ply cotton gauze* 6 wounds ; filled with six layers of calcium alginate and covered with four-ply cotton gauze	14 days
5 Calcium alginate in full thickness wounds with and without occlusion, to test the effect of reducing the amount of alginate used	4 wounds ; covered with four-ply cotton gauze* 4 wounds ; lined with one layer of calcium alginate and covered with four-ply cotton gauze 2 wounds ; covered with Op-site® dressing* 2 wounds ; lined with one layer of calcium alginate and covered with Op-Site®	5 days

*Control treatments

(a) *Calcium alginate without occlusion:*



(b) *Calcium alginate with occlusion:*



*Wounds 1 and 7 discounted because dressings became dislodged

FIG. 1 Epidermal regeneration at 3 days,

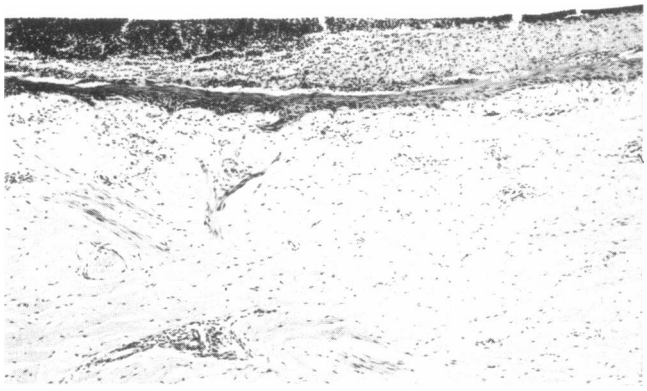


FIG. 2. Partial thickness control wound covered with Op-Site® at 3 days. Regenerating epidermis can be seen beneath a moist layer of exudate and leucocytes which has been retained beneath the dressing. H&E ×62.5

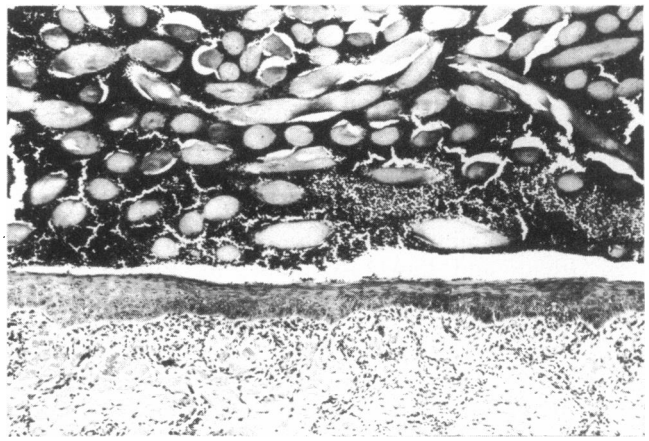


FIG. 3. Partial thickness wound covered by calcium alginate, with occlusion, at 3 days. The calcium alginate dressing is seen lying above mature regenerated epidermis. Leucocytes have penetrated the entire dressing pad. H&E ×62.5

Calcium alginate (6-ply) in full thickness wounds at 1 day. By 24 hours 4 of the wounds still had some dry calcium alginate at the top of the cavity. Histologically the wounds all showed an increased number of polymorphs compared to the control wounds. These were seen as a layer lining the cavity of the wound at the tissue/dressing interface surrounding both the fat cells and the alginate fibres. All blood still present in the wound was fully clotted and the first stages of healing could be seen. The cavities of the control wounds showed no retention of blood or exudate and were lined with only a narrow layer of blood, fibrin and polymorphonuclear cells.

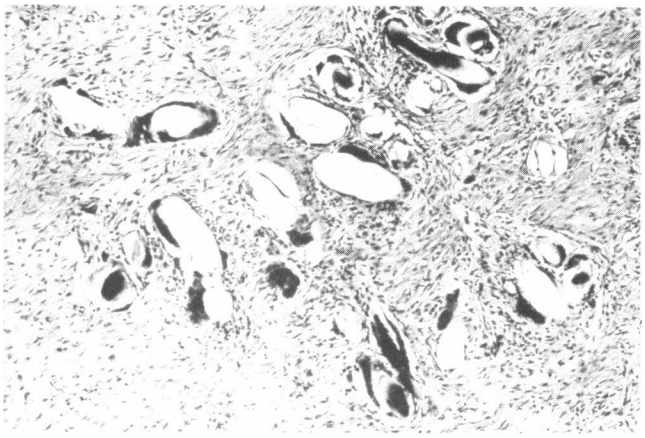


FIG. 4. Full thickness wound filled with calcium alginate, without occlusion, at 14 days. A cellular reaction to calcium alginate fibres near the base of the wound. Macrophages are seen associated with the dressing fibres. H&E ×62.5

Calcium alginate (6-ply) in full thickness wounds at 14 days. These wounds were seen to be completely filled with connective repair tissue and degrading calcium alginate fibres. In 4 of the wounds some intact fibres could still be seen and these had provoked a foreign body reaction (Fig. 4). Consequently the connective tissue repair in these wounds was less mature than in the control wounds, which were all completely filled with repair tissue. In the remaining 2 wounds a greater initial fluid loss had lead to a greater degree of fibre degradation and more advanced healing by 14 days. These 2 wounds showed 100% epithelisation and connective tissue repair at a comparable stage to the control wounds.

Calcium alginate in full thickness wounds at 5 days. As a result of the findings at 14 days less calcium alginate was used in these wounds. In this wound model 5 days is the earliest time interval where ingrowth of repair tissue would indicate any cellular responses to unwetted alginate. There was no histological evidence of delayed healing or abnormal cellular reaction in any of these wounds.

Discussion

Calcium alginate was successful in use on partial thickness wounds both with and without occlusion. Where no additional dressing pad was used to prevent dehydration the mean epidermal regeneration under calcium alginate was almost double that of the control wounds. When calcium alginate was used with occlusion the mean rate of healing was less than that seen under Op-Site® alone but the epidermis was at a more mature stage of repair than seen on the control wounds.

The experiments on full thickness wounds confirmed earlier findings with alginates; they are efficient haemostatic agents that are well tolerated by the body fluids and cellular components but, when used in cavities, the ratio of alginate to wound fluid is critical particularly in the later stages of healing. Cellular responses to unwetted calcium alginate can be seen if too great an amount is used.

In all wounds studied a greater inflammatory response was seen with calcium alginate, compared to the control wounds, in the form of an increase in the number of leucocytes. This is to be expected when biodegradable materials are employed and does not detract from the efficacy of the calcium alginate.

We conclude that further exploitation of non-woven calcium alginate as a wound dressing is indicated. It has been demonstrated that it is suitable for use as a dressing either without additional cover or in combination with a vapour permeable film. Further work is being conducted to investigate the value of using calcium alginate as a wound interface layer for composite absorbent dressings where it could act to prevent gross dehydration of the wound surface and facilitate dressing removal by prevention of dressing adhesion.

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